

REMARKS

Pursuant to 37 C.F.R. §1.111, reconsideration of the instant application, as amended herewith, is respectfully requested. Entry of the amendment is requested.

Claims 1-22 are presently pending before the Office. No claims have been canceled and applicant has added new claim 22. No new matter has been added. Support for the amendments can be found throughout the specification as originally filed. Applicant is not intending in any manner to narrow the scope of the originally filed claims.

The Examiner's Action mailed September 22, 2004 and the references cited therein have been carefully studied by Applicant and the undersigned counsel. The amendments appearing herein and these explanatory remarks are believed to be fully responsive to the Action. Accordingly, this important patent application is believed to be in condition for allowance.

Relying on 35 USC 112, first paragraph, the Examiner rejected claims 3-14 as being non-enabling for "activating a brain function". The Examiner notes that the specification is enabling for treating the diseases listed in the claims.

Applicant respectfully must disagree that undue experimentation would be required to practice the invention. Applicant directs the Examiner to page 11 for the beginning of the section "BEST MODE FOR CARRYING OUT THE INVENTION."

The specification starting at page 12 through 17 describes the experimentation related to production examples 1 and 2 and test examples 1 and 2. The results are described on page 15 and page 17 respectively. Page 15 and Fig. 1 show the results.

Method for Measuring PKC Activity in Brain:

The sample (mouse brain) was homogenized after the addition of MPBS buffer. Following homogenization PKC activity was measured using a PKC measurement kit (Pierce Colorimetric PKC AssayKit, SpinZyme format, manufactured by PIERCE).

The results are shown in Fig. 1 (U on the vertical axis represents units). In Test Lots (2), (3), (4), and (7), i.e., test lots administered with buckwheat seed powder, essence extracted from buckwheat seeds, fractionated essence having a molecular weight of 10,000 or less, an aqueous acetone solution-eluted portion of a component of the essence adsorbed in modified dextran

gel (fraction containing numerous polyphenol compounds), an increase in the amount of PKC in brain was observed as compared with the control. On the other hand, the Test Lots with the fractionated essence having a molecular weight of 10,000 or more and the water-eluted portion of a component of the essence adsorbed in modified dextran gel (fraction containing few polyphenol compounds) showed no substantial difference from the control....

The improvement in learning was judged by a test method using an 8-way radial maze. In this method, eight paths, partitioned with transparent walls, (observable from both the inside and the outside) are provided radially around a center. A feed is placed on the end of each path. A mouse that has been starved for 15 hours before initiation of the test is placed in the center of maze, where the entrance to each path gathers. The time is measured in which it takes the mouse to eat all the feeds placed on the ends of each path. The time it takes for entrance into wrong paths (that is, paths where the feed has already been eaten and no feed is present, the time of wrong response) is also measured. The 8-way radial maze was permanently placed in a room kept at a fixed environment and all the tests were performed therein. The tests were initiated on day 0 after the administration of samples for each test lot and then performed after a predetermined number of days. The results are shown in Tables 2 and 3.

(See Tables 2 and 3 on pages 16-17 of the specification)

As demonstrated in the radial 8-way maze tests and as is apparent from Tables 2 and 3, the time for correct response and number of wrong responses of the buckwheat seed essence group showed improvement over the control group and indicates that buckwheat seed essence has a positive effect on improving the ability to memorize.

Applicant believes that the above mentioned examples are evidential of the effects of the invention and contribute to enabling one skilled in the art to practice the invention. A SAM, which is a senescence-accelerated mouse, exhibits systems of aging earlier and faster than a normal mouse. As aging proceeds, memory decrease is observed in a SAM mouse. However, in the Examples of the present invention, remarkable effects of the composition of the present invention which prevented memory from decreasing were demonstrated and thereby alleviating damages to the brain by aging. Therefore, it is a reasonably derived conclusion and a proper one to consider the present invention as useful for prevention of aging symptoms, given the remarkable observations during the above described experiments.

Further, tests were conducted on humans. Tests for memorization ability were conducted where words and serial numbers had to be memorized (clearly a brain function as any lay person would understand it to be). Methods for measuring the amount of lipid peroxide and SOD activity are described on page 19 and the results are presented in Tables 4 and 5 on page 20. A summary of the results and a summary of comments from human subjects described on pages 20-23 is as follows:

As is apparent from the above results both the memorization of words and the memorization of a serial number were superior after administration of the composition of the present invention in comparison to the results obtained before administration. These results clearly demonstrate an improvement in memorization ability. Further support for the improvement in memorization ability is demonstrated in the blood lipid peroxide level test results. As shown in Table 5, blood lipid peroxide levels decreased after the administration of the composition of the present invention when compared to the blood lipid peroxide levels present before administration of the composition of the present invention. Likewise, SOD activity was enhanced indicating that memorization ability was increased. Therefore, these tests demonstrate that the composition of the present invention improves the function of the brain.

Test Example 4:

Eight healthy volunteers (6 females ages 14 to 68; 2 males ages 34 and 40) were administered capsules containing 250 mg of the composition obtained in Production Example 2 at a daily dosage of 4 capsules per day comprising a morning and evening dose of 2 capsules each, for 2 months. Each person was requested to evaluate and record changes in their emotional state and feelings. For example, subjects monitored the presence, absence or changes in self-possession, peace of mind/anxiety, stress/pressure, excitation/depression, atrophy, and impatience/irritation. In addition, physical aspects were monitored, for example, the presence or absence of insomnia/sleeplessness, and headache/heavy head, etc. These results are summarized below.

Self Evaluation by Volunteers

(1) Male (34 years old, working in computer related field)

This subject reported that he worked very hard and often felt nervous. After the initiation of taking the capsules containing the composition of the present invention he reported that his temper gradually became calmed and his ability to concentrate in all areas of his life increased.

(2) Male (40 years old, quality management professional)

Prior to taking the composition of the present invention this subject reported that he had difficulty sleeping through the night. In fact, he awoke often during the night and could not fall back asleep without listening to music. After taking the capsules containing the composition of the present

invention he reported that he is able to sleep throughout the night without interruption and he slept soundly and restfully.

(3) Females (45, 51, and 58 years old, house keepers)

Each of these women reported that they had been suffering from insomnia for a long period of time. After taking the composition of the present invention these women reported that they were able to easily fall asleep. These women expressed relief that their insomnia had disappeared.

(4) Male (14 years old, student)

This subject reported that he was irritated, agitated and nervous about his upcoming entrance examinations. He indicated that he often could not concentrate on his studies. After starting the capsules containing the composition of the present invention this subject reported he felt calm again. This subject has continued to take the composition of the present invention of his own accord.

(5) Female (21 years old, unemployed)

This subject reported that for the last few years, she had been repeatedly and alternately suffering from apastia and hyperalimementosis. This caused both the subject and her parents great concern. After taking the capsules containing the composition of the present invention she reported that she gradually felt calmer and was contemplating getting her driver's license. This subjects parents also reported an improvement in this subject.

(6) Female (68 years old, unemployed)

This subject reported that she often felt irritated. In addition, she reported that her judgment was very much influenced by her feelings. After taking the capsules containing the composition of the present invention she reported that she no longer felt irritated and her judgment was more balanced and her mental wellbeing had been restored.

As described above, the administration of the composition of the present invention has produced beneficial effects in humans. These beneficial effects include the acquisition and maintenance of calmness and an increased ability to concentrate, the dissolution of feelings of irritation, and the dissolution of insomnia, to name a few. These results show the beneficial effects the administration of the composition of the present invention has on the brain and nervous system of humans.

Clearly, the above experimentation demonstrates that the present invention improves functions related to the brain, that is, short time memory, space cognition, enhancement of the PKC activity of the brain, lowering of the LPO level in blood and increasing SOD-like activity.

Through recent studies, it is widely known that oxidation stress takes somepart in progression of conditions such as dementia and Alzheimer's dementia. This data as to the blood LPO and SOD-like activity indicates that the present invention has a protective function against

oxidation stress, and therefore can be considered to alleviate and prevent symptoms of dementia and Alzheimer's dementia through its antioxidant activity.

Relying on 35 U.S.C. §112, second paragraph, the Office has rejected the subject matter of claims 1 and 21 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicant respectfully traverses the rejection and requests reconsideration.

Applicant submits that claims 1 and 21 do define the legal metes and bounds of the invention. It is not the role of the claims to enable one skilled in the art to reproduce the invention but rather to define, for those skilled in the art the legal metes and bounds of the invention. Nevertheless, in order to advance the case to allowance, claims 1 and 21 have been amended to clarify the claim limitation issues raised by the Examiner, that is, the claimed molecular weight is that of the polymer itself, not the monomer unit.

Regarding the Examiner's comments related to claims 3-14, applicant again must disagree for the reasons described above. For example, the experiments related to memorization clearly are associated with brain activity. Similarly, the other experiments conducted are all associated with brain activity so the specification clearly support the claims language. However, applicant has amended claims 3-14 as well as independent claim 1 to reflect specifically the experimentation tests that were conducted. Withdrawal of the rejection is requested.

With respect to the definitions of R and R' in claims 16 and 21, applicant respectfully submits that the Examiner has misconstrued the chemical structure and has erroneously come to the reached conclusion. The definition of R means that both dash OH representing R and wedge OH representing R are present in the composition of the present invention and the ratio between the two is 2 (dash OH) to 1 (wedge OH), and the definition of R' means that both dash OH representing R' and wedge OH representing R' are present in the composition of the present invention and that the ratio between the two is 1 (dash OH) to 2 (wedge OH). As for the R' in the catechin unit of the lower terminal, the ratio of dash OH (α configuration) to dash OH (β configuration) is 2 to 1. That is, the definitions do not mean that there are both dash OH and wedge OH in on single R or R'.

It is respectfully submitted that claims 16 and 21 fully comply with 35 U.S.C. §112, second paragraph. Withdrawal of the rejection is respectfully requested.

Relying on 35 U.S.C. §102(b), the Examiner has rejected the subject matter of claims 1-20 as being anticipated by WO 97/36497. Applicant respectfully traverses the rejection and requests reconsideration.

Applicant respectfully submits that it is important to note that, historically, the Office and the Federal Circuit has required that for a §102 anticipation, a single reference must teach (i.e., identically describe) each and every element of the rejected claim. The Office has steadfastly and properly maintained that view.

The Examiner essentially states that the '497 reference teaches structures which can be either catechin or epicatechin in a variety of ratios, encompassing the scope of the present claims. Applicant submits that although there may appear to be similarities in relation to cacao-derived catechin and epicatechin, applicant questions whether the compositions of the present invention can reasonably be considered structurally identical to the cacao-derived structure when comparing the structure of buckwheat-seed-derived catechin and epicatechin being contained in a specific ratio, to the cacao-derived structure. Applicant has amended the independent claims to delete the open ended comprising language to "consisting essentially of" to limit the claimed invention to buckwheat seed derived structure.

The '497 publication teaches procyanidin(s) extracted from cocoa and discloses its structure. However, the cited reference does not mention structural units nor component ratio of the procyanidin structure. On the other hand, the present application clearly describes the component ratio of catechin to epicatechin in polyphenols extracted from buck wheat seeds in the specification.

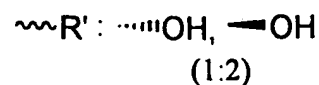
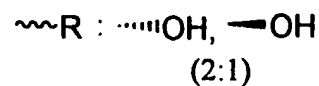
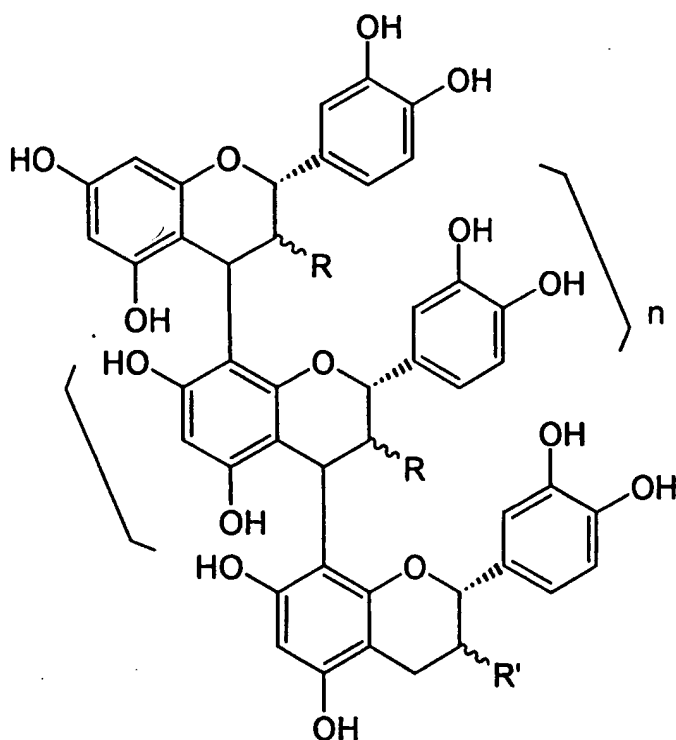
Catechin and epicatechin are stereoisomers, which have physical properties and physiological activities different from each other. Therefore, if the component ratio of catechin to epicatechin in the procyanidin of the '497 publication is different from that of the composition of the present invention, naturally, there shall be differences in the physical property and physiological property between the compositions of the two inventions (the present invention and the disclosed invention in the '497 publication).

With respect to the procyanidin of the '497 publication, only epicatechin is illustrated (in Fig. 3), and the reference is silent on the ratio of catechin to epicatechin. In fact, the reference does not present any information indicating the ratio.

With respect to the monomer compound, the '497 publication teaches the content ratio of catechin to epicatechin, 1.6% (catechin) to 38.2% (epicatechin) as disclosed in Table 4, and B-2 and B-5 dimers also comprises epicatechin. That is, the procyanidin extracted from cocoa mainly contains epicatechin in an amount larger than that of catechin.

On the other hand, the present invention discloses in detail data about the structural unit of the polyphenol polymer examined by the thiolysis method, as further described in Test 7 starting at page 25 of the specification. The results are analyzed on page 27. The formula

upper terminal



$n = 2 \text{ to } 7$

lower terminal

representing a procyanidin oligomer, indicates that the ratio of catechin to epicatechin in the upper terminal and middle is 2 to 1, and 1 to 2 in the lower terminal.

Accordingly, the total ratio of catechin to epicatechin in the polycyanidin oligomer is represented by $(2n + 3) : (n + 3)$. With the epicatechin ratio number being highest ($n = 2$), the ratio of catechin to epicatechin is 7 : 5, and therefore the content of epicatechin never exceeds that of catechin in the present invention.

Accordingly, each and every element of Applicant's claims have not been taught in that single reference. In other words, the rejected claims do not read literally on any single item of prior art because the cited reference does not teach, disclose or suggest the present invention as

claimed. Accordingly, Applicant respectfully submits that claims 1-20 and new claim 22 added herein, have not been anticipated by the '497 publication under 35 U.S.C. §102(b), and respectfully requests that such rejection be withdrawn.

Relying on 35 U.S.C. §103(a), the Examiner has rejected the subject matter of claim 21 as obvious over the '497 publication in view of U.S. Patent No. 5,232,942 based on the view that both are antioxidants. Applicant respectfully traverses the rejection and requests reconsideration.

Applicant submit that amended claim 21, which now includes the limitation of enhancing the activity of PKC, improving short term memory and alleviating degradation of space cognition, all conditions symptomatic of the aging process, overcome the rejection under 35 USC 103.

CONCLUSION

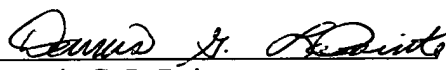
Even though the initial claims in this important patent application were drawn to a new, useful and nonobvious invention, they have now been amended to increase their specificity of language.

A Notice of Allowance is earnestly solicited.

If the Office is not fully persuaded as to the merits of Applicant's position, or if an Examiner's Amendment would place the pending claims in condition for allowance, a telephone call to the undersigned at (727) 538-3800 would be appreciated.

Very respectfully,

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